

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 2, line 29, with the following rewritten paragraph:

Figures 1A-1J depict a number of different detection chamber embodiments. Figures 1A-1F depict alternative detection chamber geometries in which the inlet port **100** is positioned at the top of the chamber. In contrast, the outlet port **101** can have several configurations. For example, in Figure 1A the outlet port is located at the top of the chamber but does not vent to the outside. In Figures 1B and 1D, the outlet port **101** is positioned at the top and vents outside. In Figure 1C, the outlet port **101** is located to the side of the chamber. In Figure 1F, the outlet port **101** comes off of the inlet port **100**. In Figures 1A through 1E, the electrode array **103** is positioned within a reaction chamber **102**, which may be formed from a gasket, a recess in the underlying printed circuit board or from the housing **104**. In Figures 1A and 1C, the reaction chamber is shaped like an inclined diamond; in Figure 1B, the reaction chamber is shaped like a diamond; in Figure 1D, the reaction chamber is circular in shape; in Figure 1E, the reaction chamber is triangular in shape; and, in Figure 1F, the reaction chamber is shaped like a square. Figure 1F depicts an embodiment in which reference electrodes **106** are located in the inlet and/or the outlet channels. The reference electrodes are preferably AgCl. The reference electrodes may be coated with AgCl before placing in the cartridge. Alternatively, a coating of AgCl may be applied to the reference electrodes while in the cartridge by applying a voltage of sufficient strength to an Ag electrode such that the silver is oxidized to form Ag⁺. Figure 1G depicts a biochip **105** comprising a reaction chamber ~~102~~ with detection chamber **113**, an electrode array **103**, a PCR chamber **115**, a

buffer chamber 170, an air pump chamber or other mechanism for moving fluid 116, one or more valves for controlling the movement of fluid 171, temperature sensors 172, heating elements integrated into the device 173, a mixing element 174, reference electrodes 106, inlet 100 and outlet 101 ports, a microchannel 110, a silicon gasket 104B with a cutout for the detection chamber 113 and a cap 130. Figure 1H depicts the top surface of an electronic biochip. The electrode array 103 is configured such that each electrode is connected via a wire lead 109 to a contact pad or interconnect 108 on the edge of the biochip. These metal contact pads can be used to make contact between the electronic biochip reader and the biochip using a standard computer edge card connector. Alternatively, as depicted in Figure 1I and 1J, the electrical connections can be made by transversing through the board to the opposite side of the substrate. The opposite side of the substrate can be arranged in the mirror image configuration to the front side, or it can be arranged in an alternative fashion. Figure 1K shows a biochip 105 with connects that transverse the board making contact with a pogo pin connector 176. The connector has an array of compliant pins 177, a circuit board housing 177, and potentially an electronic multiplexer 178. The pin grid connector ultimately plugs into an instrument through some interface like an edge card connector via metal fingers 179. In order to ensure a good connection between the pogo pin connectors and the chip, it is common to use some type of fastener.

Please replace the paragraph beginning on page 3, line 27, with the following rewritten paragraph:

Figure 2 depicts the various components that can comprise a cartridge. In the cartridge embodiment depicted in Figure 2A, the detection chamber ~~102~~ 113 contains an electrode

array 103 connected via wires 109 to interconnects 108. The array is attached to a solid surface 105 which can be made from any number of materials as described below. In addition, registration pins 107 can be attached to the biochip to enable the addition of other components. Figure 2B depicts a rubber gasket 104 with a cut out [113A] for the detection chamber 113 and registration holes 112 for attaching the gasket to the biochip depicted in Figure 2A. Figure 2C depicts a housing 114, which can be made from plastic and is attached to the biochip via registration holes 112. The cartridge 114, may optionally contain a cutout 113A for the detection chamber ~~103~~ 113 and a recessed microchannel 110 running from the inlet port 100 to the detection chamber ~~103~~ 113.

Please replace the paragraph beginning on page 20, line 8, with the following rewritten paragraph:

In a preferred embodiment, check valves are used to prevent fluid from going in and out of the reaction chamber during reactions. Generally check valves are used when in embodiments in which it is desirable to have fluids and/or air flow in one direction, but not the other. For example, when the chamber is filled and thus compressed, air and liquid flow out. Conversely, valves can be used to empty the chamber as well. Types of check valves that can be used include, but are not limited to, duck bill valves (Vernay, www.vernay.com) [www.vernay.com]), cantilevers, bubble valves, etc.

Please replace the paragraph beginning on page 21, line 9, with the following rewritten paragraph:

In a preferred embodiment, the burst valve is a film of metal or polymer. In a preferred embodiment, a free standing gold film is used, that is constructed using standard

techniques as outlined herein, by etching away a support surface. The gold membrane dissolves upon application of a voltage and Cl⁻ ions. See for example www.mchips.com [www.mchips.com]; Santini, J.T., et al., 1999, Nature, 397:335-338; both of which are incorporated by reference in their entirety.

Please replace the paragraph beginning on page 21, line 29, with the following rewritten paragraph:

In addition, commercially available valves may be used in to control the flow of liquids from into and out of the various chambers of the present invention. Examples of commercially available valves include, MEMS (micro-electro-mechanical systems) micro valves (<http://www.redwoodmicro.com>) [(http://www.redwoodmicro.com)], TiNi liquid microvalve (TiNi Alloy Company, San Leandro, CA), TiNi pneumatic microvalves (TiNi Alloy Company, San Leandro, CA), silicon micro valves (Bosch, D., et al., *Sensors and Actuators A*, 37-38 (1993) 684-692). Commercial/conventional valves also are available from Measurement Specialities, Inc., IC Sensors Division, Milpitas, CA (<http://www.msiousa.com/icsensors>) [(http://www.msiousa.com/icsensors)]; Plast-O-Matic Valves, Inc. (<http://www.plastomatic.com/>) [(http://www.plastomatic.com)], Barworth Inc. (<http://www.barworthinc.com>) [(http://www.barworthinc.com)], Mobile Electronics Solution (<http://www.mobileelectronics.net/>) [(http://www.mobileelectronics.net/)]; Specrum Chromatograph (<http://www.lplc.com>) [(http://www.lplc.com)]; all of which are hereby incorporated by reference in their entirety.

Please replace the paragraph beginning on page 22, line 4, with the following rewritten paragraph:

Other sources for obtaining valves and pumps include research foundations such as Chronos (~~<http://www.memsrus.com>~~) [<http://www.memsrus.com>]; Institute for Microtechnology - Mainz (~~<http://www.imm-mainz.de/>~~) [<http://www.imm-mainz.de/>]; Microsystems integration group - Swiss Fed. Inst. of technology (~~<http://dmtwww.epfl.ch>~~) [<http://dmtwww.epfl.ch>]; University of Washington (~~<http://lettuce.me.washington.edu>~~) [<http://lettuce.me.washington.edu>]; The Berkeley Sensor and Actuator Center (BSAC) (~~<http://www.otl.berkeley.edu/mems.html>~~) [<http://www.otl.Berkeley.edu/mems.html>]; University of Michigan, Microsystems R&D Laboratory (~~<http://www.eecs.umich.edu/MEMS/facilities.html>~~) [<http://www.eecs.umich.edu/MEMS/facilities.html>]; Caltech, MEMS Research (<http://touch.caltech.edu/home/research/files/html/researchframe.html>); all of which are hereby incorporated by reference in their entirety.

Please replace the paragraph beginning on page 24, line 1, with the following rewritten paragraph:

In addition, commercially available micro pumps may be used in to move liquid from one location to another in the cartridge. Examples of commercially available pumps include, moulded plastic micro pumps available from IMM (see ~~liganews@imm.uni-mainz.de~~) [liganews@imm.uni-mainz.de], thin film shape alloy microactuators (TiNi Alloy Company, San Leandro, CA), silicon micro pumps (see M. Richter & J. Kruckow, aktorik/paper/2000_jahresbericht/ Paper2, 16.11.00), .

Please replace the paragraph beginning on page 26, line 11, with the following rewritten paragraph:

Other embodiments include the incorporation of temperature sensors into the substrate such that the temperature throughout the board can be monitored. In a preferred embodiment, temperature sensors are created using resistive devices, including silicon diodes. Other embodiments include the use of capillary thermostats and limiters (<http://www.thermodisc.com/BulbAndCapillary.html>) [<http://www.thermodisc.com/BulbAndCapillary.html>].